Measuring substance parameters in material layer, esp. in vivo oxygen saturation in optically accessible blood containing structure

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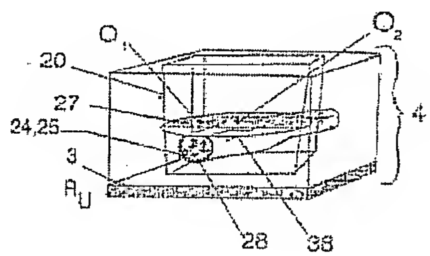
Abstract of DE **4433827** **(A1)**

The substance parameter measurement involves examining the area to be measured (20) using an ocular (7), showing one layer (27) of a vein and its vicinity (24). A confocal aperture (38) sends lights beams with varying wavelengths onto the area. Measurements of the reflection and scattering of light are taken and store in a polychromator (15). The intensity of the signals are verified and corrected if necessary by analysing two neighbouring but different areas (O1,O2). The spectral and local measurements are calculated using the following formulae : I(O, lambda)=Im(O, lambda)-K(lambda), where I(O, lambda) is the intensity of the corrected spectral and local signal, Im(O, lambda) is the intensity of the spectral an local signal, and K(lambda) is the spectral scattering light constant.; The extinction spectrum of the structure (25) is given by E(O, lambda) where E (O, lambda)=logI(O1, lambda)/logI(O2, lambda). This is followed by a non-linear compensation calculation.



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The invention relates to an arrangement and a method to the measurement of material parameters in layers of mediums, in particular to the measuring-free in vivo measurement of the oxygen saturation in optical zugängigen blood vessels. The invention is particularly suitable for reflektometrische measurements at the eye fundus and at opened organs, are zugängig optical particularly good with which the vessels. The eye fundus are however in the subsequent description only an example for any, from at least partial light transmissive layers existing medium, become described at which the extreme highly soluble method and the arrangement. The layers of the medium can have same or different states of aggregation (gaseous, liquid, fixed). Investigation object is a structure, on the one hand layers are pre-aged to which and which lies on the other hand before an arbitrary spectral reflective background. In the investigation object the relative proportions of or several components a certain can become, which differ in their spectral properties in known manner specific.

The problem definition which can be solved with the help of the invention becomes subsequent described at the example of examinations at the eye, which serve the oxygen saturation in a blood vessel for the measurement.

The oxygen saturation is the relative proportion of oxygen supporting Oxyhämoglobin at the entire hemoglobin quantity, which would be to the transport of oxygen in the blood vessel in the ply. Thus the portion of hemoglobin derivatives is not received such as Carboxyhämoglobin, Sulfhämoglobin and Hämiglobin into the calculation of the oxygen saturation. To the definition for the oxygen saturation OS the subsequent relationship applies:

EMI1.1

The different courses of the spectral extinction coefficients of Oxyhämoglobin (HbO2) and of haemoglobin (HB) in the visible spectral region are the basis for a spectrometric measurability of the single blood components. The linear weighted addition of the single component extinctions to the sum extinction coefficient of the mixing blood a possible measurement of the oxygen saturation. Bottom explicit indication of the oxygen saturation becomes the extinction hämolysierten mixing blood calculated after:
E (lambda) = c.d [epsilon HB (lambda) +OS (epsilon HbO2 (lambda) - epsilon HB (lambda))] (2).

The middle concentration C of the haemoglobin in the blood amounts to 8.9,10< -6> Mol/cm< 3>. The layer thickness D becomes indicated in cm. At the isosbestischen point with 586 Nm the decadic extinction coefficients of HB and HbO2 have the same value 7.23 10< 6> cm< 2> /Mol. In a hämolysierten blood sample, which becomes measured in a cuvette with known layer thickness, the unknowns concentration and oxygen saturation are to be only determined.

With this measurement the validity of the law of Lambert and Beer becomes assumed. The made measurement at whole blood, then arises to additional for the absorption of the haemoglobin still another scattering at erythrocytes and if necessary to the vessel wall.

For measurements at the eye fundus, which in reflectance performed to become to have to consider are further the maximum allowable exposition conditions so that in dependence of the spectral resolution with measurable radiating power of 10<,-11> W to count is. With measurement of the oxygen saturation in transmission the measurement conditions substantial are defused.

Of Hickam JB, Frayser R, Ross JC: "A study OF retinal Venous Blood Oxygen Saturation in human Subjects by photo graphics Means" in Circulation 27 (1963) 375ff became shown that the oxygen saturation is more measurable in principle in arteries and veins of the retina in the Papillengebiet. The fundus becomes in the surrounding field of the Papille with white light illuminated. Two cameras, before which interference filters with the center wavelengths of the transmission of lambda 1 = 505 are Nm and lambda 2 = 640 Nm or lambda 1 = 640 Nm and lambda 2 = 800 Nm, supply simultaneous two images of the eye fundus. One assumes the vessels are so thin that most light penetrates these and at the Papillengewebe reflected located under it becomes. Further assumed becomes that becomes regular reflected of the vessels little light. The light attenuation in the vessel is sufficient then for the law of Lambert and Beer.

From the densities of the measurement points on the vessels with lambda 1 and lambda 2 and the densities of the Papille with lambda 1 and lambda 2 the oxygen saturation bottom use of an experimental determined calibration curve calculated can become. There is the subsequent linear connection Oxygen saturation = c1 + K2.G (3).

The constants c1 and K2 depend on the container diameter and on the selected wavelength combination and become through into vitro model tests certain. The variable G becomes from the picture densities certain after

EMI3.1

Also with compliance of the diameters of vessel and capillary, largest care with exposure (parallel photography) and development, the oxygen saturation is not better than assignable with an uncertainty of +-10%. The detection of pathological changes of the oxygen saturation an uncertainty of becomes 1% desired. The need of a calibration should become avoided.

On the basis of the examinations of Pittman, R. N. and Duling B. R. (1975): "Measurement OF by cent oxyhemoglobin into the microvasculature" in J. Appl. Physiol. 321, F has 38. C. Delori: "Noninvasive technique for oximetry OF blood in retinal vessels" in Applied optics volume. 27, No. 6, 1113-1125 (1988) a method developed, possible with which the measuring-free measurement of the oxygen saturation is in retinal vessels. In addition becomes a field of approximate 1.5 mm diameter at the eye fundus successively with light of the wavelengths lambda 1 = 559 Nm, lambda 2 = 569 Nm and lambda 3 = 586 Nm illuminated. A galvanometer scanner re-paints over the multiple container profile with a field of the width of 1/5 of the container width and an height of the fivefold container width and supplies a middle profile for each used wavelength.

The principle of this method consists of the fact that the extinction of the whole blood from the extinction of the hämolysierten blood results from addition of an wavelengthindependent strewing term S:
E (lambda) = S+c.d.s. (epsilon HB (lambda) +OS [epsilon HbO2 (lambda) - epsilon HB (lambda)]) (5).

In this formula is S aselektive strewing term and s is Geometriefaktor, which considered that only a portion of the light, which steps by the vessel arrives also by the eye pupil (aperture diaphragm division) and of the detector system detected will can. This formula describes a linear connection between the measured extinction and the oxygen saturation which can be computed. The aselektive strewing term is the intersection with the ordinate, and the increase of the function becomes by concentration layer thickness geometry the product certain. The increase of equation (5) is in the whole blood because of s < 1 ever smaller as in the hämolysierten blood. After Delori the dependence of the measured extinction of the oxygen saturation is in a narrow range around 575 Nm approx. to describe 15 Nm good, if S = 0.325 and s = 0.73 become assumed. This limitation made by the assumption of an wavelengthindependent scattering.

Thus this method is not suitable to the measurement of the oxygen saturation using strong lying apart wavelengths.

▲ top

With the help of the parameters S and s can be measured, on which change of the extinction between 0% and 100% oxygen saturation is to be counted with a defined container width and with a discrete wavelength.

Table 1

Change of the extinction of whole blood in dependence of the oxygen saturation
EMI4.1

If one assumes that that the measured spectral extinction of the whole blood can become described by the extinction of the hämolysierten blood and the aselektive scattering S after equation (5), then three unknown are to be determined:

- the aselektive scattering S,
- concentration layer thickness geometry the product c.d.s and
- the sought oxygen saturation OS.

To the solution of this resultant set of equations spectral measurements are necessary with at least three wavelengths. At least a measurement must take place with a wavelength, with which the extinction coefficients differ from HbO_2 and HB. For the two other wavelengths isosbestische points can become used.

Subsequent ones become the generalized wavelengths A, b, C, D viewed. The extinction of the blood vessel for the respective wavelength becomes analytic calculated after equation (5).

On the other hand the experimental certain extinction of a blood vessel for the wavelength becomes lambda from the intensities calculated, which become on the vessel and measured in its neighbourhood:

EMI5.1

With the variables T

EMI5.2
whereby for the wavelengths A, b, C, D
A NOTE AGONY b and C NOTE AGONY D applies,
becomes for the measured extinctions and with the agreement
epsilon A (b, C, D) 1 = epsilon HB
epsilon A (b, C, D) 2 = epsilon HbO_2
the oxygen saturation according to formula (8) calculated:

EMI5.3

For isosbestische points the differences of the extinction coefficients disappear with the same wavelength in equation (8).

The requirements to the measurement system are extreme high with this proceeding. In table 1 are the changes of the extinction in the whole blood indicated, which is to be expected oxygen saturation with different container widths between 0% and 100%.

The calculation of the oxygen saturation is within a certain uncertainty z. B. 10%, 5%, 2% possible its, then must be more measurable the changes of the extinction of the whole blood, which arise in dependence of the oxygen saturation, at least also with this error. It is from basic importance that the smallest detectable change of the extinction of the detected signal and its intoxication portion is dependent.

The smallest detectable change of extinction results out:
EMI6.1

The per small signal/noise ratio SNR is, is the coarser the smallest detectable change of the extinction DELTA E. Further it is to be noted that the extinction in this equation set consists additive of the extinction of the ground and the extinction of the whole blood after equation (5). With rising entire extinction the minimum detectable change of the extinction becomes ever coarser. That is, that even with same container width, same oxygen saturation and thus same extinction of the blood with increased extinction of the ground (smaller reflectance) the oxygen saturation with a ever larger error becomes calculated. Average values for the entire extinction of the eye fundus are:

Table 2

<tb>< TABLE> Columns=2>
<tb>: Middle extinction at Fundusorten
<tb> Fundusort< September> extinction
<tb> Papille< CEL AL=L> 0.7
<tb>< UCB AL=L> papillo makuläres bundle< September> 1,7 to 2.2
<tb> Makula< September> 2,4 to 3
<tb>< /TABLE>

The bottom premiss of an ideal cooled receiver, with whom the dark portion is ID = 0, the bottom assumption of a poisson distribution registered photons noise from the root registered photons the calculated becomes. With these indications the theoretical boundary for the smallest detectable change of the extinction for each Messapparatur can become calculated.

That is, the per large intensity I0 is, which becomes measured of a model eye with white standard as eye fundus, is the larger the signal/noise ratio and all the smaller is the minimum detectable change of the extinction.

The limit for the maximum allowable exposure results from the maximum allowable irradiancy (cw-operation) or the maximum allowable energy (burst mode), which after the ANSI standard Z136.1 - 1986 fixed are. In order to be able to determine the oxygen saturation according to this method, the realized exposure must become close at the maximum allowable limit selected. In order to reach a sufficient signal/noise ratio, is to be averaged over a larger number from measurements to, which leads to a strong patient load. Patient movements during the measurements will worsen not considered and the measurement result.

By the selected Scan principle to the measurement of the light reflected of the environment and the vessel disturbing portions regular reflected light on the vessel of the strong step into appearance.

A substantial improvement of the instrumentation premisses for the measurement of the oxygen saturation became of Schweitzer and hammer by the Imaging spectrometry provided indicated in that patent application "arrangement to the spectrometric examination" (DE-P 44 10 690,4). After this principle simultaneous reflection spectra of measured become of a confocal field with an high local dissolution, scanned by all locations approach. In this way both the measurements on a vessel and the measurements are in the environment of the vessel by the same influences of noise as eyepiece transmission, fluctuations of the irradiancy etc. affected, so that their influence can become eliminated on the calculation of the optical density of the vessel. There the Imaging spectrometry becomes applied on the determination of the oxygen saturation on the principle of the three-wavelength method indicated of Delori.

It is a mechanism to the illumination with a flash lamp provided as well as in the observation path of rays an eyepiece mark before the examiner eye, whose image is congruent in the examined field with the image of an entrance gap, whereby in Messstrahlengang successively an astigmatic system, an entrance gap, a Polychromator and a detector system disposed are.

▲ top In illumination beam path is swingable a field screen, whose image is congruent in the examined field with the image of the entrance gap.

From the requirements after at least dissolvable change of extinction within a blood vessel with variable oxygen saturation, which effective entire extinctions leave themselves with ply of the vessel before different reflective Fundusorten and the theoretical detectable limiting resolution of a spectrometer In dependence of the entire extinction to conditions for the measurability of the oxygen saturation to derive.

In Fig. 1 are these connections for the wavelength 559 Nm shown. In the upper part of Fig. 1 are the saturation-independent extinction of the whole blood as well as the change of the extinction of the blood with oxygen saturations from 0% to 100% and the container widths 50 mu m, 100 mu m and 200 mu m to addition for the extinction of the Papille as ground indicated. From the respective saturation-conditional change of the extinction of the blood with different container widths the required detectable change of the extinction at fundus the calculated, which is required for the measurement of the oxygen saturation with a defined error (2%, 5%, 10%, becomes). In the bottom of Fig. 1 are the experimental certain and the theoretical smallest changes of the extinction detectable with a Imaging spectrometer in dependence of the entire extinction shown (curves).

The changes of the extinction necessary for the measurement of the oxygen saturation are likewise there registered (points). From the representation it follows that only is more measurable a practical with an error of 10%, with the Papille as ground the oxygen saturation. The examined blood vessel should be as thick ones as possible (200 mu m). The practical and the theoretical detection limit became calculated on the basis of 200 individual measurings and by summarizing 384 column pixels. It means that the oxygen saturation is not more measurable with the required accuracy also after this method.

To of Delori in Apll. Optics 27, 1113 (1988) described solution it is to be implemented that become successively used with a scannenden principle three wavelengths. The local dissolution is by the durations this Scanvorganges limited.

The light load is altogether very high.

In Delori, Pflibsen, Appl. Optics 28, 1061 (1989) made localresolved measurement, but the whole image spectral disassembled does not become.

The invention is the basis the object to develop a method and an arrangement which make it possible, measurement of material parameters of a structure covered of layers within a medium with a very high local resolution and accuracy of the material parameter (z. B. to obtain relative concentration).

In particular the oxygen saturation of the whole blood in a defined vessel despite poor signal/noise of ratio and small underground reflection with an high accuracy an not-invasive and in vivo certain is to become to be able at subjects. The measurement is to take place during minimum patient load. The influences of the rehearsing and movement and the layers before the structure which can be examined (influence of the spectral transmission of the eyepiece media) are to become reduced as far as possible.

The spectral properties of the light source and the receiver are to be likewise without influence.

The object becomes according to invention with the arrangement by the features of the 1. Claim dissolved.

The object becomes according to invention with the method by the features of the 3. Claim dissolved.

The Unteransprüche 2, 4 and 5 are advantageous embodiments.

The statement of the nature of the invention made on the basis the determination of the oxygen saturation of the whole blood by measurements at vessels, which become made at the eye fundus of a subject.

The subsequent embodiments are to be read in such a way that
the patient eye the medium,
the vessel of the structure,
the blood components the fabric,
the oxygen saturation the material parameter,
the Ophthalmolskop a Reflektometer
correspond.

The nature of the invention consists with the solve the problem of the measurement of the oxygen saturation of the whole blood in a defined vessel of the fact that the extinction of the whole blood becomes so viewed that it itself from the extinction of the hämolysierten blood, which depends on the oxygen saturation, and further from a wavelengthdependent scattering builds up, which becomes measured by simultaneous pick of the reflection spectra of a vessel and the container neighbourhood from 500 Nm to 600 Nm with a spectral resolution of small as 5 Nm with a Imaging spectrometers at least.

From the noisy measurement values with a variety of wavelengths the course of a model function certain, in that the oxygen saturation, becomes concentration layer thickness geometry a product by nonlinear compensation calculation, which becomes strewing intensity and a strewing exponent optimized, until the square error amount between the measurement values and a model function is minimized. The spectral extinction of a vessel becomes from the reflected intensity of the neighbourhood and the reflected intensity on the vessel calculated after equation (10):

EMI12.1

The intensities I (O1m, lambda) and I (O2k, lambda) are the simultaneous measured spectral intensities of light of the container environment O1m and of the vessel O2k, which became corrected with the internal equipment and the intraocular spectral stray light. The relationship, calculated after which the extinction of the whole blood measured for each wavelength after equation (10) becomes from the absorption and scattering characteristics of the blood, shows the model function according to invention after equation (11):

EMI12.2

Unknown sizes are:

- S wavelengthindependent strewing term
- c.d.s concentration layer thickness geometry product
- OS oxygen saturation
- n strewing exponent.

Substantial one is apart from the formulation of the extinction of the hämolisierten blood the formulation for the wavelength dependency of the light scattering in the whole blood

EMI12.3

The parallel measurement of the reflection spectra becomes approach a confocal Imaging Ophthalmospektrometer used, becomes illuminated with which a circular area at the eye fundus, the portions of or several vessels a covered. A spaltförmiger cutout of this range is detected on the entrance gap of a Polychromators imaged, is a disposed at whose output intensified CCD matrix, with a defined local dissolution the reflection spectra of the vessel and the environment simultaneous.

In order to ensure the confocal image of the field screen and the measuring gap on the eye fundus, a prior art system is to defective vision reconciliation in illumination beam path and in common observation and Messstrahlengang.

Since the spectral measurements become performed with smallest radiating power, strewing influences are to be considered within the measuring arrangement and within the eye. In order to seize these common, the characteristic becomes the Konfokalität exploited, after which primary only light will receive, which originates from the confocal-planar at the eye fundus. The influence of stray light works independent of it whether on an illuminated or an unlighted find-USA-real measured becomes.

▲ top From this reasons become lighting conditions different by the effect of a mechanism for the jet figuration and beam deflection generated.

In a first case a Fundusfeld becomes generated outside of the confocal measuring field (measuring gap). In a second case the measuring field (measuring gap) becomes only partial by the confocal field screen illuminated.

That bottom these conditions measured spectrum of K (lambda) is the underground spectrum, which is to be subtracted Imaging spectrum from everyone to localassociated. With this operation the underground-corrected Imaging spectrum I (O, lambda) becomes, with O - location and lambda - wavelength, obtained.

A correct measurement of the oxygen saturation requires that the entrance gap of the Polychromators is vertical aligned to the vessel which can be measured. For this object it is necessary to make a Bilddrehung of the illuminated eye fundus relative to the entrance gap of the Polychromators.

This Bilddrehung becomes achieved thereby that in the observation path of rays and measuring of the Ophthalmoskops a portion with parallel beam path is present, in which a Dove prism disposed rotatable around the optical axis is. A rotation of the prism around the angle phi an effected rotation of the image around 2 phi.

An other advantage of the inventive arrangement, become measured with which the simultaneous reflection spectra of vessel and environment with defined local dissolution, consists of it that it is not required to the determination of the optical density of the vessel, standardizing the measured spectrums on the reflectance at a white standard. It is possible to use the dynamic range of the detector system optimum.

By the inventive arrangement and the calculation according to invention of the extinction spectra of the whole blood the influences of the spectral characteristic of the light source and the receiver are eliminated. The spectral transmission of the eyepiece media is multiplicatively contained in all local resolved spectrums, so that this shortens itself after quotient formation from the result.

The spectral measurement becomes made with illumination of the eye fundus with white flashlight. Bottom these conditions is an high irradiancy allowable. Further the influence of the dark current is a so small that without a cathode cooling can be done.

If signal/noise of ratio becomes several measurements performed the improvement, then is to be counted on two error influences:

1. Change of the local situation of the illuminated and scanned field and
2. Change of the lightning intensity between the measurements.

It is to be counted by the eye movements on the fact that itself the ply of the vessel relative has changed to the pixels of the detector matrix, which corresponds to the local coordinate. This error becomes that with the Imaging spectrometer of gained images, corrected by the fact, which become in a coordinate the location information and in the other coordinate the wavelength information inertial, after correction with the underground light K (lambda) in the local coordinate after the criterion of the maximum correlation of the spectral place-dependent intensity process between the images displaced.

Fluctuations of the lightning energy between the single picks and differences in local illuminating become that becomes so made for the image areas, corrected by the fact, which are contained in all images after this situation correction as average an intensity adjustment that that integral ones of the intensity in each image certain will and the ratio of the integral intensity of each frame to the integral intensity of the brightest image formed will and each spectral place-dependent measurement value of each frame with the inverse ratio of the integral intensities becomes adjusted on the level of the brightest image.

Only after this balance different illuminating the averaging of to each other associated local and spectral intensities becomes pixelweise made. Opposite a correction of the fluctuations of the lightning energy by parallel fairs of the energy with a detector array the correction in terms of software of the lightning energy fluctuations themselves supplies at least a result better around the factor "2" at the model eye. Further the advantage exists that local differences in the Fundusbeleuchtung by the integral intensity adjustment balanced become.

The displacement of the Imaging spectrums, which leads same structures to the coverage, effected a simultaneous reduction of the influence of the regular reflectance of the structure (on the vessels) in the calculation of the material parameters (oxygen saturation). The influence of the regular reflectance on the determination of the oxygen saturation can become further by a model calculation corrected. For this the intensity profile, which results from the spectral absorption of the blood, is copied thus by a smoothing function that an optimum matching develops after the criterion of the smallest error square sum. This correction can become both for the measured single spectra and and remainder correction at the averaged image after the image position shift and the balance of intensity fluctuations performed.

As next step the influences of the spectral characteristic of the lamp, you receiver system and all layers of the eye eliminated after equation (10), become which affect similar on the vessel and its neighbourhood.

EMI15.1

According to these correction calculations the extinction spectrum of the whole blood in a vessel is present. With each wavelength measured extinction E (lambda) is a value on the left side of equation (11). The number of the measuring wavelengths large is according to invention as the number of the unknowns. Thus a system from t+r equations is present to the calculation of the t unknowns. With the analytic calculation the t unknown out only t equations becomes the result for the oxygen saturation substantial by the intoxication portions corrupted, since each measurement value consists also after the correction of a correct portion and an intoxication portion.

Made the according to invention calculation of the oxygen saturation after a nonlinear balance procedure. Equation (11) becomes so formulated that the oxygen saturation, concentration layer thickness geometry the product, which is wavelengthindependent strewing intensity and the strewing exponent parameters which can be optimized. With the so formulated equation the course of the measured extinction spectrum is approximated. The best solution of the set of equations for these four parameters is in the minimum of the error square sum between model function and corrected measurement values achieved.

For measurements at the eye convenient is to limit the model calculations to the range of safe measurement values. That is, measurement values for wavelengths smaller as 500 Nm remain unconsidered. It is sufficient to evaluate only the wavelength range between 500 Nm and 600 Nm since in this range the differences of HB and HbO2 are most favourably more measurable.

By the invention process of the matching of a model function to out corrected reflection measurements a calculated extinction spectrum the effective signal/noise ratio is improved approximately around the root from the number of the used supporting places.

The measurement method according to invention and the arrangement make possible that the measurement independent

- of the spectral properties of the ground of the measuring object (the plane of measurement, eye fundus),
- of the spectral properties of the mediums before the measuring object (eyepiece media),
- of the spectral characteristic of the radiation source and
- become of the spectral properties of the measuring arrangement, in particular of the spectral characteristic of the receiver performed.

On the basis the measurement of the oxygen saturation described arrangement and the method are more applicable also for the measurement of the oxygen saturation in blood vessels, which exposed during an operation became.

In same way the nature of the invention refers to the solution technical objects, how

- are subject the contactless measurement of the material concentrations in a pipeline, to their optical environmental conditions of a continuous change or
- Concentration measurements in a Glasschmelze, with which the disturbing influences of the convection of the ambient air are to be switched off and from Flammenbildern.

▲ top

The invention becomes subsequent described on the basis embodiments. Show:

Fig. 1 confrontation of required, practical realizable and theoretical attainable smallest detectable change of the extinction to the measurement of the oxygen saturation,

Fig. 2 generalized description of the measuring object,

Fig. 3 arrangement to the measurement,

Fig. 4a Nichtüberdeckende ply of entrance gap of the Polychromators and image of the confocal diaphragm at the eye fundus,

Fig. 4b covering ply of entrance gap of the Polychromators and and image of the confocal diaphragm at the eye fundus,

Fig. 5 partial coverage of the entrance gap of the Polychromators by the image of the confocal diaphragm with central ply between both,

Fig. 6 approximation of the container profile with constant wavelength by a smoothing function to the balance of regular reflectance on the vessel,

Fig. 7 selection of the measuring points on the vessel and in its environment,

Fig. 8 measured spectrums of vessel and environment,

Fig. 9 approximation of the extinction spectrum of the whole blood of a vessel by a model function,

Fig. 10 comparison between spectrometrically oxygen saturation measured with the suggested arrangement in an arteriole of the pig brain and the laboratory-chemical certain arterial oxygen saturation,

Fig. 11 comparison between spectrometrically oxygen saturation with the laboratory-chemical certain oxygen saturation from a Hirnvene, measured with the suggested arrangement in a Venole of a pig brain.

Fig. 1 represents the need of an improved measuring technique and an improved method. The fig is in the conditions of the technique described.

In Fig. 2 is the measuring object described. In a medium, here the patient eye 4, existing from layers, a structure 25, here a vessel 24, is before a ground, here the eye fundus 3, which have the reflectance Ru. In the structure 25 is a fabric 28, here blood, of which spectrometrically and contactless parameters, here the oxygen saturation, certain to become to be supposed. The survey area 20 is the range of the medium, here the patient eye 4, 17 evaluated from which light becomes by a detector system 16 detected and of a computer (see in addition Fig. 3).

The image 38 of a confocal field screen 37 or 33 develops during radiography of the survey area 20 with the light of a flash lamp 9 on the structure 24. From this preferably circular illuminated field a rectangular measuring field 27 congruent over an astigmatic system 13 becomes on the entrance gap 14 of a Polychromators 15 imaged. The light based on different locations (O1 beside the structure and CO2 on the structure) becomes disassembled spectral as complete spectrum for both locations simultaneous parallel. By this measurement principle the spectral influences of the ground, the detector, the radiation source remain and the transmission of the pre-aged layers without influence on the measurement result. After correction by the stray light, which develops in the survey area 20 and in the metre, the extinction spectrum of the fabric becomes 2B (whole blood in the vessel 24) certain from the quotient of the reflection spectra of the environment of the structure and from the structure 25 after Logarithmieren. With a suitable model function the course of this extinction spectrum is approximated in such a way that parameters of the fabric (oxygen saturation of the whole blood) with high accuracy certain to become to be able.

Fig. the arrangement points 3 to the measurement of material parameters by means of designed the according to invention Reflektometers, in the example a measuring Ophthalmoskop (retina camera).

It becomes first a first variant for the unit the jet figuration and beam deflection 34a described. The mechanism for the jet figuration and beam deflection 34 is 36 constructed from a fixed confocal field screen 37 and a swing-out glass plate.

A surrounding field lighting 1 illuminated over the deflecting mirrors 10 and 11 the eye fundus 3 of the patient eye 4 with continuous light. After the principle of the aperture diaphragm division the made reflex-free observation of the eye fundus 3 by the examiner eye 6. By swinging the deflecting mirror 12 the eye fundus 3 become 15 imaged on the entrance gap 14 of a Polychromators. By the effect of an astigmatic system 13 only a narrow strip of the eye fundus 3 of the entrance gap 14 of the Polychromators becomes 15 received. Before the examiner eye 6 an eyepiece mark 7 in the observation path of rays 5, which is congruent to the measuring field, is, which is 4 fixed of the entrance gap 14 of the Polychromators 15 at the eye fundus 3 of the patient eye. This image is in x-direction, which corresponds to the gap-high, so extended that it at least a retinal main vessel including its environment covered.

The investigation place at the eye fundus 3 becomes 2 set by switching on of the surrounding field lighting 1 on into the illumination beam path, as the deflecting mirror 10 swung and the measuring field 27 of the eyepiece mark becomes 7 positioned on the field which can be examined.

The deflecting mirror swung 12 from the observation path of rays 5 out. In illumination beam path 2 is in a mechanism for the jet figuration and beam deflection 34 a confocal field screen 37, which is so adjusted that the image of the entrance gap 14 of the Polychromators 15 is because of the eye fundus 3 of the patient eye 4 central within the circular image 38 of the confocal field screen 37 at the eye fundus 3. This field screen 37 can be either fixed in the part illumination beam path 2 disposed, only by the light of the flash lamp 9 is through-radiated or this field screen is in illumination beam path 2 in a range swingable disposed, which is through-radiated common by the light of the flash lamp 9 and the surrounding field lighting 1. In the mechanism for the jet figuration and beam deflection 34, which are in illumination beam path 2 disposed, an inclined/slanted swing-out plan plate 36 is in light direction toward the confocal field screen 27 in a parallel beam path. A picture-rotary Dove prism 35 is in a parallel beam path of observation path of rays 5 and Messstrahlengang 26 rotatable disposed around the optical axis.

In to the eye fundus 3 of the patient eye 4 congruent an image plane illumination beam path 2 is a movable interior fixation mark 19. Of eye fundus the 3 reflected light, which arrives over the swung deflecting mirror 12 and the astigmatic system 13 by the entrance gap 14 into the Polychromator 15, disassembled becomes in the Polychromator. At the output of the Polychromators 15 is a low light detector system 16, which contains a CCD matrixEmpfängeranordnung.

If assumed becomes that in x-direction the lines run and in y-direction the columns, then each receiver element in column direction detects a monochromatic part of the spectral disassembled light for each pixel location, which is dissolvable by the number of the receiver elements in x-direction. A computer 17 of the processed received signals and represents these at a display 18.

The simultaneous pick of the spectrums for all locations in x-direction the eye fundus 3 with flashes become from a flash lamp 9 over the deflecting mirror 11 illuminated. For the period of the flash the deflecting mirror is 10 swung from the beam path.

The width of the entrance gap 14 certain in connection with the dispersing characteristics of the Polychromators 15 and the size of the matrix elements in y-direction the spectral resolution. The size of the matrix elements in x-direction certain bottom consideration of the scale between the retina of the patient eye 4 and the retina picture in the plane of the entrance gap 14 of the Polychromators 15 the local resolution at the eye fundus 3, whereby to the image of the entrance gap 14 of the Polychromators 15 on the eye fundus 3 an astigmatic system 13 is in Messstrahlengang 5 disposed.

By an astigmatic image in x and y-direction achieved becomes that to the entrance gap of the Polychromators bottom keeping a measuring field corresponds to the aperture of the Polychromators at the eye fundus, whose expansion is in x-direction of the required expansion, at least associated as upper covering of a vessel and its neighbourhood. The expansion of the measuring field in y-direction becomes a so selected that the gap width of the entrance gap of the Polychromators a spectral resolution of approximately 3.5 Nm possible.

The measurement of the oxygen saturation made after the subsequent flow: The patient eye 4 becomes 1 irradiated with the surrounding field lighting. With fixation of the patient eye 4 on the movable interior fixation mark 19 the eye fundus 3 so aligned become that an interesting vessel 24 of the measuring field 27, which becomes image of the eyepiece mark 7, at the eye fundus 3 covered. By tricks of the Dove prism 35 around an angle phi the image of entire eye fundus 3 becomes so aligned that the measuring field 27 cuts the interesting vessel 24 vertical (Fig. 4b). Subsequent one the made measurement of the underground intensity, which is predominant caused by strewing influences in the apparatus and in the eye.

For this the inclined/slanted plan plate 36 becomes, in the arrangement the jet figuration and beam deflection the 34 (Fig.), into the illumination beam path 2 swung, the deflecting mirror 10 finds 3, detail 34a tilted and the eye fundus 3 with the white light of the flash lamp 9 so illuminated that the

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measuring field 27 at the eye fundus and illuminated field at the eye fundus 3, approved by likewise do not overlap the confocal field screen 37 located in the arrangement to the jet figuration and beam deflection 34, (Fig. 4a).

The measurement of the spectral reflectance of vessel 24 simultaneous with its environment made in the interesting wavelength range so that the plan plate 36 swung out and the interesting portion of the vessel becomes 24 9 so illuminated with the flash lamp that from there reflected light in the measuring field 27 becomes on the entrance gap 14 of the Polychromators 15 imaged and 16 registered after spectral dismantling in the Polychromator 15 of the detector system.

After these operations the underground spectrum and the localresolved Imaging spectrum are present of the vessel 24 and of its environment. Fig. 8 shows as example the spectrums, which became of a vessel and measured of its environment. The underground spectrum becomes the balance of the disturbing internal stray light of each measured spectrum subtracted.

Thus the corrected localresolved reflection spectrum results
Industrial union (lambda) =Im (CO2, lambda) - k (lambda) for the vessel
and
IU (lambda) =Im (O1, lambda) - k (lambda) for the environment of the vessel.

The improvement signal/noise of ratio becomes several Imaging spectrums of the interesting vessel 24 received. The balance of patient end fixations the underground-corrected Imaging spectrums become to each other displaced after the criterion of the maximum correlation along the local coordinate x. After this operation only a part is contained of the picture matrix as average in all partial images. The balance of fluctuations of the irradiancy between the measurements calculated becomes wavelengthbased integral ones of the intensity for each on the average all images contained image part place and. The intensity of each pixel of an image becomes multiplied with the quotient from the integral intensity of the brightest image and the integral intensity of the viewed image.

Subsequent one becomes from the displaced and scaled Imaging spectrums a pixelweise average value regulation made.

From the illumination of the vessel 24 bottom different angles the container reflexes at different locations result, so that after the container situation correction relative is to the pixels of the picture matrix the influence of the regular reflectance on the averaged image reduced.

The elimination of remaining regular container reflection 41 can become by approximation of the measured container profile 39 with a smoothing function 40 achieved, those the extinction of the vessel 24 over the cross section of the vessel with constant wavelength describes (Fig. 6). After this operation the made calculation of the extinction spectrum of the vessel filled with blood 24.

For this the corrected reflection spectrum of the container environment is logarithmiert by the corrected reflection spectrum of the vessel divided and subsequent (equation 10) (see Fig. 9). With high oxygen saturation the spectral course of the extinction spectrum of Oxyhämoglobin significant is more recognizable in this extinction spectrum of the whole blood in the vessel. This partially strong noisy extinction spectrum of the whole blood in the vessel 24 is approximated subsequent in a nonlinear compensation calculation by the model function after equation (11). For this the parameters strewing intensity S, concentration layer thickness geometry product become c.d.s, the strewing exponent n and the oxygen saturation OS changed until the minimum of the square error amount between the extinction spectrum of the whole blood is 43 in the vessel 24 and the model function 42 achieved (Fig. 9).

The results of a such spectrum approximation are in table 3 indicated.

Table 3

Results of the approximation of the extinction spectrum of whole blood by the model function after equation (11)
EMI22.1

The efficiency of the presented method to the measuring-free in vivo measurement of the oxygen saturation in optical zugängigen vessels became checked at the animal model bottom different artificially respirating conditions. The spectrometric measurements became simultaneous at an arteriole and at a Venole of a pig brain performed. Comparative measurements made by laboratory-chemical determination of the oxygen saturation of the left-ventricular and the brain-venous blood. Fig. 10 shows a linear connection between in vivo measured arterial oxygen saturation values and the laboratory -chemical certain oxygen saturation values of the left-ventricular blood. The spectrometrically not-invasive 45 DEG bottom in the arteriole certain values lie within a tolerance volume of +-4% around the ideal straight one.

In Fig. 11 represented connection 45 DEG bottom between spectrometrically in vivo certain oxygen saturation in a Hirnvenole and the laboratory-chemical certain oxygen saturation values from a Hirnvene shows a systematic deviation of -1,6% of the ideal straight one. The measurement values lie within a tolerance volume of +-2%.

The mechanism for the jet figuration and beam deflection 34 can in a second variant after Fig. 3 also so performed its that in it a movable confocal field screen is 33 disposed, their image to the measurement of the underground spectrum (internal equipment and intraocular stray light) with the illumination of the eye fundus 3 of the patient eye 4 the measuring field 27 not covered (Fig. 3, detail 34b, Fig. 4a).

To the measurement of the spectrum of vessel and environment the movable confocal field screen is 33 into such a position guided (Fig. 3, detail 34c, Fig. 4b) that their image at the eye fundus the measuring field complete and central covered. The measurement of the underground spectrum and the spectrum of vessel and environment can take place parallel, if the fixed confocal field screen 37 the measuring field 27 central, but only partial covered (Fig. 5). By the unlighted measuring fields 31 on both sides of the confocal illuminated measuring field 30 the underground spectrum (internal equipment and intraocular stray light) becomes simultaneous with the reflection spectrum of vessel 24 and its environment measured, measured by the illuminated measuring field 30.

The balance of fluctuations of the lightning energy of the flash lamp 9 within a Messfolge can take place also in such a way that a light measure 32 measures with each illumination of the eye fundus 3 with light of the flash lamp 9 their energy and the intensity with the quotient, measured thereby of each image pixel of the detector system 16, becomes from the largest lightning energy within a screen sequence and the lightning energy with the pick of the viewed Imaging spectrum in the computer 17 multiplied.

In order to reach a confocal image of the measuring field 27 and the image 38 of the confocal field screen 33 or 37 at the eye fundus 3, are in illumination beam path 2 and in the observation path of rays and measuring 26 and 5 simultaneous acting prior art arrangements to the balance of the defective vision of the patient eye 4 disposed.

Reference symbol list
1 surrounding field lighting
2 illumination beam path
3 eye fundus (fundus)
4 patient eye
5 observation path of rays
6 examiner eye
7 eyepiece mark
8 field screen (swingable)
9 flash lamp (lightning lighting)
10 deflecting mirrors (swingable)
11 deflecting mirror (hole mirror)
12 deflecting mirrors (swingable)
13 astigmatic system
14 entrance gap
15 Polychromator
▲ top
16 detector system
17 computers

18 display
19 interior fixation mark
20 survey area
21 image of the entrance gap of the Polychromators at the eye fundus
22 Papille
23 Fovea
24 vessel
25 structure (vessel 24)
26 Messstrahlengang
27 measuring field (at the eye fundus 3, image of the eyepiece mark 7)
28 fabric
29 center
30 illuminated measuring field
31 unlighted measuring field
32 light measure
33 movable confocal field screen
34 mechanism for the jet figuration and beam deflection
35 rotatable Dove prism
36 swing-out plan plate
37 fixed confocal field screen
38 image of the confocal field screen
39 container profile
40 smoothing function
41 regular container reflection
42 model function for the spectral extinction process of the whole blood in the vessel
43 extinction spectrum of the whole blood in the vessel

Symbol
OS oxygen saturation
CHb concentration of the sauerstoffreien haemoglobin
CHbO2 concentration of the Oxyhämoglobins
lambda WellenlängeE (O, lambda) localresolved ExtinktionsspektrumE (O) localresolved extinction process with constant WellenlängeE (lambda) extinction spectrum epsilon HB molar decadic extinction coefficient of haemoglobin epsilon HbO2 molar decadic extinction coefficient of Oxyhhämoglobin
C total concentration of haemoglobin and Oxyhämoglobin in the blood
D layer thickness (container width)
C1, K2 constants
G variable
T variable
S wave (prolonged) independent strewing term
s Geometriefaktor
A, b, C, D different wavelengths
R reflectance
RU reflectance of the environment of the vessel
I measured intensity
I0 of a model eye with white standard measured IntensitätIm (O, lambda) intensity of the measured place and wavelengthresolved SignalsI (O, lambda) intensity of the measured place and wavelengthresolved corrected SignalsId (lambda) intensity of the dark current, corresponds to the underground spectrum of K (lambda)
Jmax largest integral intensity of the imaging spectrums
Ji integral intensity of the viewed imaging spectrum
IE EingangsintensitätIU (lambda) corrected measured intensity from the environment of the GefässesIG (lambda) corrected measured intensity of the vessel DELTA P movement of the fixation mark for the interior fixation DELTA E smallest still detectable ExtinktionsänderungSNR signal/noise ratio
sigma scattering
phi angles of rotation of the Dove prism
psi tilt angle of the PlanplatteK (lambda) spectral stray light in the medium and in the arrangement (underground spectrum), corresponds to ID (lambda)
K (O, lambda) localresolved spectral stray light in the medium and in the arrangement
O location
O1m of locations in the environment of the structure (vessel)
O2k of locations on the structure (vessel)
x local coordinate
t number of the unknowns in the set of equations (11) t+r number of the equations to the calculation of the t unknowns
n strewing exponent

1. Arrangement to the measurement of material parameters,
with an observation path of rays (5),
a detection path of rays (26), in which a Polychromator (15) with an entrance gap (14) is,
whereby the Polychromator (15) a detector system (16) is downstream, a simultaneous localresolved measurement in a first direction and a spectral resolved measurement in a second direction the allowed, whereby the localresolved measurement is parallel aligned to the entrance gap,
with illumination beam path (2) with a field screen (33, 37) and a lighting device (9), the light with at least three wavelengths delivers, whereby an eyepiece mark (7) in the observation path of rays (5) and the entrance gap (14) congruently and sharp become into the plane of the image (38) of the field screen (37) imaged and their image (21, 27 '), which becomes partial a measuring field defined, by the image of the field screen (33, 37) covered, whereby detection path of rays and observation exhibit a common portion, is disposed in which a picture-rotary Dove prism.

2. Arrangement according to claim 1, with a mechanism for beam deflection, it the allowed to shift for a second measurement the image (38) of the field screen in such a way that does not become the measuring field defined by the image of the eyepiece mark and the image entrance gap illuminated.

3. Method to the measurement of material parameters, using an arrangement after one of the claims 1-2,
whereby at least once an illumination of a portion of the measuring field with light
at least three wavelengths made,
at least a first measurement of of the spectral intensity distribution in the illuminated range of the measuring field with an high local dissolution (in (O, lambda) the made and at least a second measurement of of the spectral intensity distribution (K (lambda) in the unlighted range of the measuring field made,
whereby for each selected measurement point a subtraction of of the measured of the spectral intensity distribution (K (lambda) in the unlighted range of the measuring field (31) of measured the intensity distribution in the illuminated range of the measuring field (30) (in (O lambda) for each wavelength (lambda) and each location (O) in the illuminated range of the measuring field (30) (according to the formula
I (O, lambda =Im (O, lambda) - K (lambda))
made,
in order to produce corrected localresolved spectral intensity distributions,
whereby becomes selected in the illuminated range of the measuring field (30) at least one measuring point (O1m), which is not appropriate for structure which can be examined on one and which becomes localresolved extinction spectrum of the structure by the fact calculated that the quotient from the spectral intensity distribution at this selected measuring point (O1m) and the localresolved spectral intensity distributions for locations (O2K) on the structure formed and subsequent is logarithmiert, according to the formula:

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4. Process according to claim 3, whereby first and the second measurement take place with a partial coverage of the measuring field via the image of the field screen simultaneous.

5. Process according to claim 3, whereby the second measurement temporal after the first measurement made, after the image of the field screen became so displaced that the measuring field does not become illuminated.

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